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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,898	11/28/2000	Leroy Hood	P-IS 4403	7808

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EXAMINER	
AGRAWAL, RITESH	
ART UNIT	**PAPER NUMBER**
1631	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	09/724,898	HOOD ET AL.	
	Examiner	Art Unit	
	Ritesh Agrawal	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-9,11,13,15,16,65,70-80,90,95-104,138,139,141 and 143-189* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-9,11,13,15,16,65,70-80,90,95-104,138,139,141 and 143-189* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' amendment and request for reconsideration in the communication filed on 1/26/07 are acknowledged and the amendments entered.

Claims 1, 6-9, 11, 13, 15, 16, 65, 70-80, 90, 95-104, 138, 139, 141, 143-189 are currently pending and under consideration.

Withdrawn Rejections

2. The prior rejection (page 7, line 11 through page 9 of the office action mailed 7/26/06) of claims 8, 72, and 96 under 35 U.S.C. 112, 1st paragraph, an enablement rejection, is hereby withdrawn in light of applicants' arguments (remarks, pages 19-20).

The prior rejection of claims 8, 72, 74, 78, 96, 98, 102, and 151 under 35 U.S.C. 112, 2nd paragraph, an indefiniteness rejection, is hereby withdrawn. The rejection of claims 72, 74, 78, 96, 98, 102, and 151 is withdrawn in light of applicants' amendment filed 1/26/07. The rejection of claim 8 is withdrawn in that it was erroneously listed as being rejected.

Specification

3. The specification is objected to because of the following:

The use of the trademark WINDOWS has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. It can be found, for example, on page 126 of the specification.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

As this is just exemplary of trademarks present in applicants' specification, applicants are requested to thoroughly search the specification and modify all trademarks present therein.

Appropriate correction is required. This objection is newly applied.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1, 6-9, 11, 13, 15, 65, 70-79, 90, 95-103, 141, 143-152, and 154-189 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are directed to a method for determining a comparative expression profile comprising steps of creating a multidimensional space, determining multidimensional coordinate points, determining a health-associated reference expression region, comparing coordinate points, and determining whether the coordinate point is within of the health-associated reference region. Claims 65,90, and 144 further comprise a step of determining expression levels of molecules.

However, not all processes are statutory under 35 U.S.C. 101. *See Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility.* 1300 *O.G.* 4, on 22 November 2005 (published at the USPTO web site http://www.uspto.gov/web/patents'patog/week47/OG/TOC.htm). To satisfy 101 requirements, the claim must be for a practical application, which can be met if the claimed invention "transforms" an article or physical object to a different state or thing OR the claimed invention otherwise produces a useful, concrete, and tangible result. If claims are directed to abstract ideas (such as mathematical algorithms), natural phenomena, and laws of nature, the claims must be considered as a whole for determining whether an abstract ideas, natural phenomena, or laws of nature has a particular application.

In the instant case, the claimed method does not transform or reduce an article or a physical object (e.g., array signals) to a different stage or thing because the "result" of the method (i. e., a multidimensional coordinate point in multidimensional space) is merely data (expression information) and is not equivalent to physical transformation. The claims do not recite tangible expression (i. e., real-world result) of determining the location of a multidimensional coordinate point in multidimensional space in a form useful to one skilled in the art. Thus, the method does not recite steps of producing something that is concrete, useful, and tangible, and is not statutory.

Claims 141 and 143 are directed to a computer-readable medium or carrier wave comprising instructions for performing the method of claim 1. A carrier wave is not a physical product and is therefore nonstatutory subject matter. The specification does not

define a computer readable medium as a physical product, thus a computer readable medium may be a carrier wave, and is not necessarily a physical object. As neither the claimed computer readable medium or carrier wave is necessarily a physical "product," claims 141 and 143 are rejected as not being directed to statutory subject matter.

This rejection is reiterated from the previous Office action mailed 7/26/06. Applicants' arguments have been fully considered, but they are not found persuasive.

Applicants argue:

> First, Applicants respectfully submit that the claims are directed to statutory methods and are not directed to the so-called "judicial exceptions" of an abstract idea, law of nature or natural phenomenon (remarks, page 15).

However, applicants' methods simply recite a series of computational steps using abstract mathematical ideas with the application of those ideas to data without a requirement for "real-world" actions. As such, applicants claimed methods are not covered by the statutory methods.

Applicants further argue:

> Rather, the tangible requirement does require that the claim must set forth a "practical application" that produces a "real-world result." . . . Applicants respectfully submit that the claimed methods are directed to a useful invention that is practically applied in determining the health state of an individual in comparison to a reference population based on the expression levels of molecules (remarks, page 16).

However, as applicants themselves admit, the statutes require that the *claim* must set forth a practical application that produces a "real-world" result. There are no claimed steps that produce a real-world result. Applicants' claimed methods simply result in the determination of a theoretical location of a "coordinate point." This, in and of itself, is not a real-world result.

With respect to claim 141 applicants argue:

> It is clear that the claims are not directed to "nonfunctional descriptive material" such as music, literary works or a compilation or mere arrangement of data." Accordingly, Applicants respectfully submit that claim 141, which recites a computer readable medium, should be considered statutory subject matter, as clearly stated in the MPEP (remarks, pages 16-17).

While applicants' claim is not drawn to "nonfunctional descriptive material", given applicants' disclosure, applicants' definition of computer readable medium is reasonably interpreted to include carrier waves. As computer instructions, per se, represent non-statutory subject matter, and carrier waves represent non-statutory subject matter (as discussed below) applicants' claim to a computer readable medium is interpreted to include computer instructions encompassed in a carrier wave. Since at least one embodiment of the claimed invention is non-statutory, the rejection is maintained.

With respect to claim 143 applicants argue:

> To the contrary, a carrier wave is an electromagnetic wave and therefore is a physical entity. Furthermore, the MPEP acknowledges that "on some computer-readable medium, in a computer or on an electromagnetic carrier wave" are alternatives for recording descriptive material (remarks, page 17).

Despite applicants' assertions, just as the air that serves as the medium for transport of an electromagnetic wave is not a physical entity, neither is the wave itself. As applicants themselves cite (see remarks, page 16), the passage from the MPEP in which the carrier waves are discussed is directed towards *non-statutory* subject matter. In fact, applicants' own citation from the MPEP, "When functional descriptive material . . . it becomes structurally and functionally interrelated . . . " (remarks, page 16), points out the importance of a structural interrelationship between the computer, the computer readable medium, and the functional descriptive material. As neither a carrier wave nor

a set of instructions has a structural component, embodiment of computer instructions within a carrier wave does not meet the requirements for statutory subject matter.

5. Claims 1,6-9, 11, 13, 15-16,65,70-80,90,95-104, 138-139, 141, and 143-189 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility.

Claim 1 is directed to a method of determining a comparative expression profile in an individual comprising creating a multidimensional space related to expression levels of molecules, determining a multidimensional point for reference and test individuals, determining a health-associated region for the reference individuals, comparing a multidimensional coordinate point of the individual to the health-associated region of the reference population, and determining whether the multidimensional coordinate point of the individual is outside of the health-associated region which indicates a perturbed expression profile. Claims 90 and 144 are directed to a method of diagnosing a health states in an individual comprising similar steps. The specification on pages 1 and 3 discloses that the instant invention is useful for predictive medicine and efficiently diagnosing a disease based on a gene expression pattern in an individual. However the disclosed utility is not applicable to the instant claims. For example, the claimed methods "determine" whether an expression profile of an individual is "perturbed" from the comparison to a profile to the "health-associated" reference population. Neither the specification, not the claims disclose any information about "health-associated" reference individuals and/or what the "health-associated" reference

indicates, *e.g.,* reference individuals are healthy, carry disease markers, carry markers specific for a particular stage of a disease, carry markers for specific alleles, carry ancestral markers, *etc.* Determining that an individual has a "perturbed" profile without knowing what a reference represents does not provide any information about a disease stage or health conditions of the individual, and therefore does not allow one skilled in the art to "effectively diagnose a disease." Thus, the claimed method does not have a "result" which is "of immediate benefit" because one skilled in the art would not know what "perturbed" profile indicates. Consequently, the instant claims do not have substantial utility (a "real world" use) because the methods do not have a stated correlation between, for example, a disease and a determined perturbation and is not particular to a specific health condition. Therefore, determining what a "perturbed" expression profile indicates would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. The instant invention also does not have a specific utility, because absent any disclosure about, for example, a stage of health or disease and/or allelic markers in a affected and unaffected population, and whether the "reference profile" represents a healthy or diseased, or specific subpopulation, *etc. (i.e.,* absent some correlation between a specific population and disease to be diagnosed), the asserted utility is not specific. No such information is recited in the instant claims and further research would be required to determine such a correlation. Applicant is reminded that a "use" to perform further research is not a utility under 35 U.S.C. 101.

Claims 138-139, 14 1, and 143 are directed to a computer system and a computer readable medium performing steps of the instant methods. Because the method does not have a specific, substantial and credible utility for the reasons set forth above, any computer system and/or program implementing such a method also lacks utility. The system and a computer readable medium in this case perform a method which produces no useful result, and one of ordinary skill in the art would not know for what purpose or to what useful end such a system might be used for, therefore, the invention lacks utility.

For the reasons stated above claims 1,6-9, 11, 13, 15-16,65,70-80,90,95-104, 138-139, 141, and 143-189 lack patentable utility under 35 U.S.C. 101.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1,6-9, 11, 13, 15-16,65,70-80,90, 95-104, 138-139, 141, and 143-189 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The above rejections are reiterated from the prior Office action. Applicants' arguments have been fully considered, but they are not found persuasive.

Applicants argue:

> The specification teaches, for example, on page 5, line 25, to page 6, line 16, that the methods of the invention can be used in a multiparameter analysis by measuring the expression levels of multiple molecules representative of the health state of an individual (remarks, page 17).
>
> The specification further teaches, for example, on page 6, line 2 1, to page 7, line 3, that the methods of the invention are advantageous in that they can be used to predict the health state of an individual by determining whether the individual has a reference expression profile indicative of a reference health state or a perturbed expression profile indicative of a potential disease state in the individual or of a predisposition to developing a disease (remarks, page 18).
>
> To the contrary, it is clear from the teachings of the specification that a "perturbed expression profile" refers to a characteristic representation of the expression state of a sample of molecules of a population that falls outside a health-associated reference expression region, that is, statistically differs from the reference population (page 28, line 15, to page 29, line 11). Furthermore, such information can be used to determine the health state of an individual, including whether a person has expression levels that fall within those of a reference population, for example, a population of healthy individuals, or outside of the reference population and is in a "perturbed" health state (page 29, line 18, to page 30, line 9). The methods are useful for predictive and preventative medicine and therefore clearly have a specific, substantial and credible utility (remarks, page 19).

Despite applicants' assertions, the claimed invention lacks patentable utility because it lacks specific and substantial utility. While applicants point to possible uses for their claimed invention, all such uses (e.g. a "health state") are general – applicants fail to point out a single specific (e.g. a single disease, condition, etc.) use for which one could readily apply applicants' claimed invention. Furthermore, given the generality of the claimed method, it is not of immediate benefit because one would have no idea of what molecules (genes, proteins, metabolites, etc.) to test for a given "health-state" unless they were to carry out considerable research to identify those molecules. As applicants themselves point out, a "reference profile" could be either healthy or diseased (remarks, page 18, third paragraph). Therefore, one of skill in the art would not

know what a "perturbed" profile indicates as it could indicate either the presence or absence of disease.

As argued above, since the methods have no specific, substantial, and credible utility, neither do the computer, computer readable media, and carrier waves that employ the method.

7. Claims 90, 95-104, 144-152, and 172-189 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Independent claims 90 and 144 have been amended to include the limitation of "thereby diagnosing a health state in an individual" using the multidimensional analysis of molecule expression levels. The specification, however, does not adequately describe how to diagnose any health state using a multidimensional analysis of molecule expression levels, as claimed by applicants.

In analysis of claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, regarding genus/species situations, the written description guidelines note that "satisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register:

December 21, 1999 (Volume 64, Number 244), revised guidelines for written description, which can be obtained from the USPTO website: <http://www.uspto.gov>). Given that the genus essentially includes almost any health state, there are no common attributes or features of the elements possessed by the members of the genus in view of the large number of species. In fact, certain health states are not caused by changes in molecule expression levels, but are caused by other types of mutations (e.g. missense mutations). As applicants' claimed invention is drawn to diagnosing health states by quantifying the amount of molecules, applicants could not have diagnosed any health state as claimed. Furthermore, given that applicants do not disclose how to use their claimed invention to diagnose any specific health state, one skilled in the art would have reasonable doubt that applicants had possession of the claimed genus at the time the application was filed.

This rejection is newly applied, but applied in response to applicants' amendment to independent claims 90 and 144.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 90, 95-104, 144-152, and 172-189 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is newly applied, but necessitated by amendment.

Independent claims 90 and 144 have been amended to include the limitation "thereby diagnosing a health state in an individual" in step (g). It is unclear if the terms "health state" and "individual" refer to the same "health state" and "individual" as is previously recited in the claims.

Conclusion

9. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ritesh Agrawal whose telephone number is (571) 272-2906. The examiner can normally be reached on 8:30 AM - 5:00 PM M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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SUPERVISORY PATENT EXAMINER